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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/541,019	06/28/2005	Akira Tsuji	Q88424	4031

23373 7590 03/31/2008

SUGHRUE MION, PLLC
2100 PENNSYLVANIA AVENUE, N.W.
SUITE 800
WASHINGTON, DC 20037

EXAMINER	
PALENIK, JEFFREY T	
ART UNIT	PAPER NUMBER
1615	

MAIL DATE	DELIVERY MODE
03/31/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/541,019	TSUJI ET AL.	
	Examiner	Art Unit	
	Jeffrey T. Palenik	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14 and 17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 June 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *16 Sept 2005, 9 Mar 2007 and 11 Apr 2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Remarks

Applicant's election without traverse of Group I, claims 1-14 and 17, in the reply filed on 8 January 2008 is acknowledged.

Claims 15, 16, 18 and 19 are hereby withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 7 January 2008.

The remaining claims 1-14 and 17 are presented and represent all claims under consideration.

Information Disclosure Statement

Three Information Disclosure Statements filed 16 September 2005, 9 March 2007, and 11 April 2007 are acknowledged and have been reviewed.

Specification

The abstract of the disclosure is objected to because it refers to non-elected subject matter. Correction is required. See MPEP § 608.01(b).

Claim Objections

Claims 10 and 11 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to

cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Each of the aforementioned dependent claims is directed to subject matter other than the claimed composition. Dependent claims 10 and 11 are directed to pH-based limitations required of the proton-coupled transporters that allow for optimal performance. Since the limitations cited in the dependent claims are not directed to the claimed, the aforementioned claims are interpreted herein, for the purposes of examination on the merits, to read as "the pharmaceutical composition of claim 1".

Claim 9 is objected to because of the following informalities: the amino acid "glycin" is misspelled and should be corrected to reflect "glycine". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Independent Claim 1 and dependent claims 2-14 and 17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter that is not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Claim 1 is drawn to a pharmaceutical preparation comprising "a compound recognized by a proton-coupled transporter and a pH-sensitive polymer". While the examiner acknowledges that the terms "compound," "proton-coupled

transporter," and "pH-sensitive polymer," are mentioned in the instant specification, but the terms are neither defined nor related to one another by the instant specification in a clear and concise manner (i.e. which compounds are recognized by which proton-coupled transporters). As such, the disclosure of the instant specification is not sufficient to support the generic concept of "a compound recognized by a proton-coupled transporter and a pH-sensitive polymer" and requires further clarification.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1-14 and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation "a compound recognized by a proton-coupled transporter and a pH-sensitive polymer" in claim 1 is not clear because it is uncertain whether the pH-sensitive polymer recognizes the compound of the composition or if the pH-sensitive polymer is part of the actual composition. For the purposes of examination on the merits, the broadest reasonable interpretation accorded herein by the Examiner is: a composition comprising a.) a compound which is recognized by a proton-coupled transporter and b.) a pH-sensitive polymer.

The term "excellent" in claim 1 is a relative term which renders the claim indefinite. The term "excellent" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The term renders vague and indefinite, the dosage

parameter "gastrointestinal absorbability" making it unclear how much or to what degree absorption needs to take place in order to be within the scope of the invention.

The recitation "comprising a compound recognized by a proton-coupled transporter and a pH-sensitive polymer" in claims 1 and 17 is unclear. The language of the claims renders the limitation indefinite because it is not clear whether the pH-sensitive polymer is part of the compound doing the recognizing or a part of the compound being recognized. For the purposes of examination on the merits, the limitation will be interpreted by the Examiner to mean that the composition comprises both 1) a compound recognized by a proton-coupled transporter and 2) a pH-sensitive polymer.

The term "optimum" in claims 1 and 17 is a relative term which renders the claims indefinite. The term "optimum" is not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The term renders vague and indefinite, the amount of pH-sensitive polymer sufficient to effect cellular uptake of the compound, especially since different compounds of the invention will differ structurally and therefore not be equally accepted by the receptors. For the purposes of examination on the merits, this limitation will be interpreted to mean that *any* amount of a pH-sensitive polymer need only be present in the compound in order to "optimally" enable cellular uptake of the compound.

Regarding the limitation to the compound recognized by the amino acid transporter in claim 9, the scope of the number of members recognized by the transporter is unclear since the parenthetically referred to group at the end of the claim remains open. Furthermore, it is unclear

from the language of the limitation whether either or both "L-alanine" and "-alanine" are within the intended scope of the claim.

Claim 13 contains the trademark/trade name "Eudragit". Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe methacrylic acid copolymer compounds and, accordingly, the identification/description is indefinite.

Applicant is advised that should claim 12 be found allowable, claim 13 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

The remaining claims 2-8, 10-12 and 14 are also rejected since they depend from claim 1.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-7, 12-4 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Behl et al. (U.S. Patent 4,525,339).

The instant claims 1 and 17 are drawn to a gastrointestinally-absorbed, pharmaceutical preparation comprising 1) a compound recognized by a proton-coupled transporter and 2) a pH-sensitive polymer. Dependent claims 2-4 are directed to a peptide-specific proton-coupled transporter. Dependent claim 5 further limits claim 4 by reciting compounds recognized by the peptide transporter. Dependent claim 6 recites limitations to the composition of claim 3 such that the proton-coupled transporter is a monocarboxylic acid transporter. Dependent claim 7 further limits claim 6 by reciting compounds recognized by the monocarboxylic acid transporter. Claims 12 and 13 both recite limitations to the pH-sensitive polymer of the composition. Claim 14 recites the composition of claim 1, further limiting it to an oral dosage form.

Behl et al. teaches an orally administered enteric coated pharmaceutical composition which consists essentially of a beta-lactam antibiotic admixed with an enhancer consisting of a C_2 to C_{12} glyceride mixture with fatty acids having a length of C_2 to C_{12} (claim 1). Examples of C_2 to C_{12} fatty acids admixed with glycerides that are taught include butyric acid (col. 10, lines 20-30). Table 3 also teaches the use of monoglyceride of acetic acid (e.g. Enteral monoacetin). Enteric coatings that are taught include methacrylic acid copolymers L and S (e.g. Eudragit L and S) (col. 10, lines 58-65; col. 11, lines 1-30).

Claims 1-3, 8, 9, 12-14 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Gaunt (U.S. Patent 3,148,124).

The instant claims 1, 12-14 and 17 are drawn to an orally administered, gastrointestinally-absorbed, pharmaceutical preparation, as described above. Dependent claims 2, 3 and 8 are directed to a peptide-specific proton-coupled transporter (e.g. amino acid transporter). Claim 9 recites compounds recognized by the amino acid transporter transporting D-cycloserine (e.g. glycine).

Claims 1 and 6 of Gaunt teach the preparation of oral dosage formulations comprising water-soluble medicaments further comprising at least one non-reactive water-soluble carrier such as glycine. pH-Sensitive polymers such as polyacrylic acid derivatives are taught as alkali-susceptible materials useable in combination with the medicament of the dosage (col. 5, lines 39-52). The dosage is further taught to be solubilized by alimentary fluids, first being penetrated by gastric fluids, but then increasing the rate of penetration by the intestinal fluids such that the active medicament is largely released in the intestines (col. 5, lines 39-48).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-9, 12-14 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Behl et al. (U.S. Patent 4,525,339) in view of Gaunt (U.S. Patent 3,148,124).

The instant claims are drawn to an orally-administered, gastrointestinally-aborbed, pharmaceutical preparation, as described above.

Such compositions are taught by Behl et al., as earlier described.

Behl et al., however, does not teach the limitation of the instant claims wherein compounds are recognized by amino acid transporters transporting D-cycloserine such as alanine, L-proline, or glycine.

The invention of Gaunt teaches the preparation of oral dosage formulations comprising water-soluble medicaments further comprising at least one non-reactive water-soluble carrier such as glycine and pH-sensitive materials (e.g. polyacrylic acid), also as described above.

In view of the combined teachings of the prior art, one of ordinary skill in the pharmaceutical art would have been motivated to prepare an enteric-coated drug formulation whose composition contained both a compound recognized by a proton-coupled transporter and a pH-sensitive polymer with a reasonable expectation of controlling the release of the admixed medicament. Such would have been obvious in the absence of evidence to the contrary because

Behl et al. teaches glycol compounds as alternative enhancers to compounds such as butyric acid (col. 2, lines 16-29). Gaunt teaches water-soluble glycol as an alternative carrier to glycine, in claim 6. Therefore, modification of the invention of Behl et al. to substitute glycine for a glycol compound as a release enhancer is well within the purview of the skilled artisan. Furthermore, a person of ordinary skill in the art would have been motivated, with minimal undue experimentation, to make the necessary result-effective modifications thus enabling the required delay of drug release from the composition by adjusting parameters such as the compound recognized by the transporters in the small-intestinal epithelial cells, and reasonably would have expected success because the prior art teaches the mixing of different combinations of pH-sensitive polymers and compounds recognized by cellular transporters.

No claims allowed.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey T. Palenik whose telephone number is (571) 270-1966. The examiner can normally be reached on 7:30 am - 5:00 pm; M-F (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be

obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jeffrey T. Palenik/
Examiner, Art Unit 1615

/Michael P Woodward/
Supervisory Patent Examiner, Art Unit 1615